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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,915	04/27/2001	Paul David Robbins	AP32737-072396.0225	1483

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,915	ROBBINS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *35-40,60-62,66 and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34,41-59 and 63-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5 and 6*
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

Claims 1-34, 41-59 and 63-65 are pending in the instant application.

Election/Restrictions

Applicant's election of Group I (claims 1-34, 41-59 and 63-65) in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 35-40, 60-62, 66 and 67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Claims 1-34, 41-59 and 63-65 have been examined as indicated below.

Claim Objections

Claim 26 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, claim 26 has not been further treated on the merits.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

SEQ ID NO. 1 (c) culturing the dendritic cells and (d) administering the tolerogenic dendritic cells to the host; further comprising incubating the dendritic cells in the presence of one or more cytokines; wherein the cytokine is GM-CSF; further comprising incubating the dendritic cells in the presence of TGF-β; further comprising infecting the tolerogenic dendritic cells with a viral vector before administering the cells to the host; further comprising administering FK506 to the host; further comprising administering cyclosporine A to the host; further comprising administering FK506 and cyclosporine A to the host; wherein the host is a transplant host; wherein the host has an inflammatory related disease; wherein the host has arthritis.

Storm et al. teach methods of inhibiting rejection of a transplanted tissue in a mammal and inhibition of autoimmune related tissue destruction by introducing into a cell DNA comprising at least one comprising regulatory element including a synthetic regulatory DNA sequence from at least one of NF-κB, NF-IL-6, IL-6, LRE, AP-1, p91/stat, or the IL-6 response elements (see claims 1, 2, 5, 16 and 18). Storm et al. also teach that a host responds to transplanted material though a complex series of cellular interactions among T and B lymphocytes and dendritic cells (see pagl 1, [006]). Storm et al. further teach the mammal is a mammal with rheumatoid arthritis (see claim 6).

Storm et al. do not teach a method for enhancing tolerogenicity in a mammal host comprising (a) propagating immature dendritic cells from a mammalian donor, (b) incubating the dendrite cells with an oligodeoxyribonucleotide having at least one NF-κB binding site under conditions wherein the dendritic cells internalize the oligodeoxyribonucleotide; wherein the oligodeoxyribonucleotide has the sequence set forth in SEQ ID NO. 1 (c) culturing the dendritic cells and (d) administering the tolerogenic dendritic cells to the host; further comprising

Claims 1-6, 7-14, 41, 42 and 43-48 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-6, 7-14, 41, 42 and 43-48, drawn to "[a] tolerogenic dendritic cell", reads upon a naturally occurring dendritic cell, which is a product of nature that does not clearly show the "hand of man". Language at the beginning of these claims such as "an isolated dendritic cell" would remove the instant rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-25, 27-34, 41-59 and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storm et al. [U.S. Publication No. US2002/0164311 A1] in further view of Thomson et al. [U.S. Patent No. 5,871,728] Lu et al., (Journal of Leukocyte Biology, 1999 Vol.

66:293-296) Lu et al. (Gene Therapy, 1999 Vol. 6:554-563) and Bielinska et al. (Science, 1990 Vol. 250:997-1000).

Claims 1-6, 7-14, 41, 42 and 43-48 are drawn to a tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector; wherein the viral vector is derived from a virus selected from the group consisting of adenovirus, adeno-associated virus, retrovirus and herpes virus; wherein the oligodeoxyribonucleotide sequence has two NF-κB binding sites; wherein the oligodeoxyribonucleotide has the sequence set forth by SEQ ID NO. 1 and a method of producing a tolerogenic dendritic cell comprising propagating immature dendritic cells from a mammalian donor, (b) incubating the dendrite cells with an oligodeoxyribonucleotide having at least one NF-κB binding site under conditions wherein the dendritic cells internalize the oligodeoxyribonucleotide; wherein the oligodeoxyribonucleotide has the sequence set forth in SEQ ID NO. 1 (c) culturing the dendritic cells, further comprising incubating the dendritic cells in the presence of one or more cytokines; wherein the cytokine is GM-SCF, further comprising incubating the dendritic cells in the presence of TGF-β further comprising infecting the tolerogenic dendritic cells with a viral vector; wherein the viral vector is derived from a virus selected from the group consisting of adenovirus, adeno-associated virus, retrovirus and herpes virus Claims 15-25, 27-34, 49-59 and 63-65, are drawn to a method for enhancing tolerogenicity in a mammal host comprising (a) propagating immature dendritic cells from a mammalian donor, (b) incubating the dendrite cells with an oligodeoxyribonucleotide having at least one NF-κB binding site under conditions wherein the dendritic cells internalize the oligodeoxyribonucleotide; wherein the oligodeoxyribonucleotide has the sequence set forth in

incubating the dendritic cells in the presence of one or more cytokines; wherein the cytokine is GM-CSF; further comprising incubating the dendritic cells in the presence of TGF-β; further comprising infecting the tolerogenic dendritic cells with a viral vector before administering the cells to the host; further comprising administering FK 506 to the host; further comprising administering cyclosporine A to the host; further comprising administering FK 506 and cyclosporine A to the host.

Thomson et al. teach enhancing tolerogenicity in a mammal host comprising propagating immature dendritic cells from a mammalian donor, culturing the dendritic cells and administering the tolerogenic dendritic cells to the host (see claim 1). Thomson et al. further teach incubating the dendritic cells in the presence of one or more cytokines, wherein the cytokine is GM-CSF (see claim 8) and incubating the dendritic cells in the presence of TGF-β, FK506 or cyclosporine A (see column 8, lines 23-25).

Lu et al. teach immunosuppressive molecules such as TGF-β can be genetically engineered in dendritic cells. Lu et al. further teach manipulation of dendritric cells by exposure to TGF-β via adenoviral vectors, can confer tolerogenic properties (see page 294, last paragraph).

Lu et al. teach adenoviral delivery of alone does not affect the expression of costimulatory molecules. Lu et al. further teach surface expression of MHC class II and costimulatory molecules (CD40, CD80 and CD86) was not inherently affected by transduction with adenovirus infection (see page 555, third paragraph).

Bielinska et al. teach regulation of gene expression with double-stranded phosphorothioate oligonucleotides of NF-κB (see Abstract). Bielinska et al. further teach an

oligodeoxyribonucleotide identical to that of SEQ ID NO. 1 of the instant invention (see page 1000 #19).

It would have been *prima facie* obvious to one of ordinary skill in the art to make a tolerogenic dendritic cell comprising an oligonucleotide having one or more NF-κB binding sites because Storm et al. a tolerogenic dendritic cell comprising an oligonucleotide having one or more NF-κB binding sites inhibit autoimmune related tissue destruction in a mammal. One of ordinary skill in the art would have been motivated to make a tolerogenic dendritic cell comprising an oligonucleotide having one or more NF-κB binding sites because the prior art has taught such cells inhibit rejection of a transplanted tissue in a mammal (Storm et al.). One of ordinary skill in the art would have expected success in making a tolerogenic dendritic cell comprising an oligonucleotide having one or more NF-κB binding sites because Bielinska et al. explicitly taught such compounds regulate gene expression.

It would have been *prima facie* obvious to one of ordinary skill in the art to devise a method for enhancing tolerogenicity in a mammal because Storm et al. taught methods of inhibiting rejection of a transplanted tissue and inhibition of autoimmune related tissue destruction in a mammal by introducing into a cell DNA comprising at least one comprising regulatory element of NF-κB response element. One of ordinary skill in the art would have expected success in making DNA comprising at least one regulatory element of NF-κB response elements since the prior art has explicitly taught such compounds regulate gene expression (Bielinska et al.) One of ordinary skill in the art would have been motivated to devise a method for enhancing tolerogenicity in a mammal because the prior art has taught inhibiting rejection of

a transplanted tissue in a mammal can prevent graft rejection following organ transplantation (Storm et al).

It would have been obvious to one of ordinary skill in the art to propagate immature dendritic cells from a mammalian donor, culture the dendritic cells and administer the tolerogenic dendritic cells to a host because Thomson et al. explicitly taught such methods can effect dendritic cell maturation and hence enhance the immune response of a host mammal. One of ordinary skill in the art would have been motivated to propagate immature dendritic cells from a mammalian donor, culture the dendritic cells and administer the tolerogenic dendritic cells to a host because Thomson et al. taught these methods enhance tolerogenicity to foreign graft in a mammal. One of ordinary skill in the art would have been motivated and expected success in incubating the dendritic cells in the presence of one or more cytokines and pharmaceuticals because the prior art has taught these factors act as immunosuppressive agents in enhancing tolerogenicity. One of ordinary skill would have been motivated to infect tolerogenic dendritic cells with an adenovirus viral vector before administering the cells to the host because Lu et al$_1$. taught TGF-β gene transfer using adenovirus enhances tolerogenic potential and adenovirus infection does not affect costimulatory molecule expression (Lu et al$_2$).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

icg
November 27, 2002

SEAN McGARRY
PRIMARY EXAMINER